Real-world pharmacovigilance of tobramycin/dexamethasone: A safety signal analysis using the the Food and Drug Administration Adverse Event Reporting System (FAERS)

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Abstract

Background

Tobramycin/dexamethasone is a widely used topical ophthalmic combination of aminoglycoside antibiotic and synthetic glucocorticoid. Its real-world post-marketing safety profile, especially regarding rare adverse events, demographic disparities, and temporal toxicity patterns, remains incompletely characterized.

Methods

This retrospective pharmacovigilance study analyzed data from the Food and Drug Administration Adverse Event Reporting System (FAERS) (2004 first quarter–2025 second quarter), including reports designating the drug as primary suspect. Disproportionality analyses (Reporting Odds Ratio, Proportional Reporting Ratio, Bayesian Confidence Propagation Neural Network, Multi-item Gamma Poisson Shrinker), subgroup (gender, age, reporter type) and time-to-onset analyses (Weibull distribution) were conducted.

Results

A total of 1,085 primary suspect reports (3,338 distinct adverse events) were included. Eye Disorders was the predominant System Organ Class (44.55%, Reporting Odds Ratio = 39.41, 95% confidence interval: 36.79 – 42.21). Core adverse events included Eye Pain (n = 117, Reporting Odds Ratio = 43.46), Intraocular Pressure Increased (n = 62, Reporting Odds Ratio = 90.59), Ocular Hypertension (n = 36, Reporting Odds Ratio = 380.03), and rare severe Corneal Exfoliation (n = 14, Reporting Odds Ratio = 3243.77). Males, pediatric (< 18 years) and elderly (≥ 65 years) patients had higher adverse event risks. Median time-to-onset was 13 days (interquartile range: 2 – 15 days), with 88.08% of adverse events within 1 month and Weibull shape parameter = 0.521.

Conclusions

This study comprehensively characterizes the drug’s safety profile, confirming known ocular risks and identifying underrecognized severe adverse events. Demographic and temporal patterns support personalized monitoring, providing data-driven evidence to optimize post-marketing risk management.

1. Introduction

Tobramycin/dexamethasone is a cornerstone topical ophthalmic combination formulation, integrating the bactericidal activity of tobramycin (an aminoglycoside targeting Gram-positive and Gram-negative ocular pathogens) and the potent anti-inflammatory effects of dexamethasone (a synthetic glucocorticoid). It is widely prescribed for steroid-responsive ocular inflammatory conditions complicated by superficial bacterial infections (e.g., conjunctivitis, keratitis) and post-surgical inflammation, owing to its synergistic efficacy in mitigating infection and inflammation simultaneously(1–4). Despite its long-term clinical use, the post-marketing safety profile of this combination remains incompletely characterized, particularly in real-world settings.

Existing safety data are primarily derived from controlled clinical trials, which are limited by strict inclusion/exclusion criteria, small sample sizes, and short follow-up durations(1, 4). These trials have confirmed common ocular adverse events (AEs) such as local irritation and intraocular pressure (IOP) increased but fail to capture rare/long-term AEs, demographic-specific risk patterns (e.g., age- or gender-related disparities), and temporal characteristics of toxicity—critical gaps for guiding personalized clinical monitoring. For instance, dexamethasone is known to elevate IOP, but the magnitude of this risk in vulnerable populations (e.g., pediatric, elderly patients) and its association with severe ocular sequelae (e.g., corneal damage, glaucoma progression) lack real-world quantification(5). Additionally, as a combination product, the independent and synergistic contributions of tobramycin and dexamethasone to adverse reactions have not been systematically evaluated in large-scale datasets.

Spontaneous adverse event reporting systems, such as the Food and Drug Administration (FDA) Adverse Event Reporting System, offer a valuable resource for post-marketing pharmacovigilance, providing large-scale, long-term real-world data on drug-associated AEs across diverse populations(6–8). Disproportionality analysis using validated algorithms (Reporting Odds Ratio [ROR], Proportional Reporting Ratio [PRR], Bayesian Confidence Propagation Neural Network [BCPNN], Multi-item Gamma Poisson Shrinker [MGPS]) enables the detection of potential safety signals, including unrecognized or rare reactions(9, 10). Subgroup and time-to-onset (TTO) analyses further reveal population-specific risks and temporal patterns of toxicity, which are unavailable in traditional clinical trials.

Against this backdrop, the present study aimed to systematically characterize the post-marketing safety profile of tobramycin/dexamethasone using the FDA Adverse Event Reporting System (FAERS) data spanning over 21 years (2004Q1–2025Q2). Guided by the Reporting of a Disproportionality Analysis for Drug Safety Signal Detection Using Individual Case Safety Reports in PharmacoVigilance (READUS-PV) guidelines for disproportionality analysis(11, 12), this study sought to: (1) identify and prioritize AE signals at the System Organ Class (SOC) and Preferred Term (PT) levels; (2) explore gender-, age-, and reporter-type-specific AE patterns; (3) analyze the temporal distribution of AEs to optimize monitoring timelines; and (4) provide data-driven evidence to refine clinical risk management strategies for this widely used ophthalmic formulation.

2. Materials and Methods

2.1 Data sources

This study investigated AEs linked to tobramycin/dexamethasone as documented in the FAERS. The dataset spanned from the first quarter of 2004 to the second quarter of 2025 (2024 Q1 – 2025 Q2), which is retrievable through FAERS' official online download platform (https://fis.fda.gov/extensions/FPD-QDE-FAERS/FPD-QDE-FAERS.html). To optimize retrieval comprehensiveness, a systematic search strategy was adopted by integrating the drug's MeSH term with its corresponding brand names. FAERS encompasses seven core data modules—specifically Demographic and Administrative Records (DEMO), Drug Exposure Details (DRUG), MedDRA-coded Adverse Reaction Information (REAC), Patient Clinical Outcomes (OUTC), Report Source Metadata (RPSR), Drug Therapy Timelines (THER), and Indications for Use (INDI)-that collectively facilitate multidimensional pharmacovigilance assessments, such as temporal signal detection and population-specific risk stratification.

2.2 AEs and drug identification

All AEs in FAERS were classified according to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms (PTs)(13).. The study assessed the incidence and severity of tobramycin/dexamethasone-related AEs at both the SOC and PT levels of the MedDRA hierarchy. Relevant reports were identified using both the drug's generic and brand names. To ensure analytical accuracy, the study restricted to entries in which tobramycin/dexamethasone was designated as the Primary Suspect (PS) drug. Additionally, duplicate entries were eliminated in adherence to FDA recommendations: for cases sharing identical Case Identifiers (CASEIDs), the record with the most recent FDA_DT was retained; when both CASEID and FDA_DT were identical, the entry with the higher PRIMARYID was selected. Clinical features of FAERS reports involving tobramycin/dexamethasone were summarized, and characteristics of serious versus non-serious cases were further documented.

2.3 Disproportionality and Subgroup analysis

Disproportionality analysis was utilized to detect potential correlations between tobramycin/dexamethasone and AEs, leveraging four well-validated statistical algorithms to ensure robust signal detection. The Reporting Odds Ratio (ROR), a frequentist statistical method, was selected due to its computational simplicity and resistance to nonselective underreporting of AEs—a common limitation of spontaneous reporting systems(14). The PRR, another widely adopted frequentist approach, was included to supplement ROR by quantifying the disproportionality between the target drug and specific AEs relative to the broader FAERS dataset(15). In instances of sparse AE documentation, two Bayesian methods were employed: the BCPNN and the MGPS. BCPNN integrates Bayesian principles into 2×2 contingency table analyses, enabling reliable early signal detection even with limited case numbers(16), while MGPS applies shrinkage estimation to stabilize signal estimates, maintaining high detection power in datasets with rare events(17).

To characterize population-specific AE risk patterns for tobramycin/dexamethasone, stratified subgroup analyses were conducted based on three clinically relevant variables, with cases lacking age data excluded. For age stratification, patients were divided into three groups consistent with clinical practice and demographic research: <18 years (pediatric/adolescent), 18–64 years (adult), and ≥ 65 years (elderly). For gender, reports were categorized into male and female. For reporter type, stratification followed FAERS' predefined categories: consumer and healthcare professional. The same panel of four disproportionality algorithms used in the overall analysis was applied to each subgroup. This methodological consistency ensured valid cross-group comparisons, with the primary objective of uncovering population-specific AE patterns that might be masked in the unstratified dataset.

2.4 Time-to-onset analysis

The date of AE occurrence (EVENT_DT) and the start date of tobramycin/dexamethasone administration (START_DT) were extracted from REAC module data. TTO of AEs was determined by the equation: Time to onset = EVENT_DT − START_DT. The median (interquartile range, IQR), minimum–maximum values, and Weibull shape parameter (WSP) test were applied to assess the TTO data for tobramycin/dexamethasone. A duplicate removal procedure was also performed, invalid data were excluded, and only reports with available TTO information were included in the analysis. The WSP test evaluates TTO characteristics and can describe the non-uniform incidence rate of AEs (i.e., whether the risk increases or decreases over time). The selection of the shape parameter and differentiation criteria have been detailed in prior studies(18).

2.5 Clinical prioritization of signals

Relevant AE signals were classified and prioritized using a semi-quantitative scoring system that incorporated four key metrics: clinical relevance (based on Important Medical Event/Designated Medical Event (IME/DME) lists), reporting frequency, signal stability across analyses, and reported case fatality rate. Signals were subsequently stratified into low (0–2 points), moderate (3–5 points), and high (6–8 points) priority tiers for further evaluation(19).

2.6 Software and tools

All data processing and statistical analyses were performed with SAS 9.3 and R version 4.3.1. Result visualization was achieved via the R package ggplot2.

3. Results

3.1 Descriptive analysis

A comprehensive query of the FAERS database from 2006 to 2025 identified 22,775,812 adverse event reports. After deduplication, 1,085 reports listed tobramycin/dexamethasone as the PS drug, corresponding to 3,338 distinct AEs (Fig. 1A). From 2004 to 2012, annual adverse event reports of tobramycin/dexamethasone remained at a relatively low level (mostly below 30). A continuous upward trend emerged from 2013 to 2024, with reports climbing steadily year by year. By 2024, the number of AE reports had risen sharply, reaching a peak (close to 150) in 2024 (Fig. 1B).

Based on the analysis of 1,085 reports from the FAERS database, the clinical characteristics of AEs associated with tobramycin/dexamethasone are detailed in Table 1. The cohort was predominantly female (61.5%, n = 667), with males accounting for 30.7% (n = 333) and gender data missing in 7.8% (n = 85) of cases. In terms of age distribution, adults aged 18 to < 65 years constituted the largest subgroup (31.9%, n = 346), followed by elderly individuals aged ≥ 65 to ≤ 85 years (22.2%, n = 241), pediatric patients < 18 years (4.6%, n = 50), and those > 85 years (2.8%, n = 30); age data was missing in 38.5% (n = 418) of reports. Consumers were the primary reporting source (41.7%, n = 452), followed by physicians (19.4%, n = 211) and other health professionals (19.4%, n = 211), while pharmacists accounted for 3.0% (n = 33) and lawyers for 0.4% (n = 4). Geographically, most reports originated from the United States (46.7%, n = 507), followed by China (18.8%, n = 204) and France (5.4%, n = 59). Notably, 50.2% (n = 545) of reports were classified as serious, with fatal outcomes (Death) documented in 0.6% (n = 7) of cases; the most frequent non-fatal outcomes included other events (36.4%, n = 395) and hospitalization (9.4%, n = 102).

As shown in Table 2, among 1085 FAERS reports, 50.2% (n = 545) of tobramycin/dexamethasone-related adverse events (AEs) were serious and 49.8% (n = 540) non-serious, with distinct distributions across gender, age, weight, and reporter subgroups. Gender-wise, females had higher proportions of both AE types and remained the largest group in serious AEs due to higher overall reporting volume. For weight, normal-to-moderate weight patients (≥ 50–≤100 kg) had the highest serious AE proportion (155/545, 28.4% vs. 74/540, 13.7% non-serious), followed by low weight patients (< 50 kg, 32/545, 5.9% vs. 8/540, 1.5%), while high weight patients (> 100 kg) showed no significant difference (6/545, 1.1% vs. 4/540, 0.7%). Age stratification revealed the highest serious AE proportion in adults 18–<65 years (237/545, 43.5%), followed by elderly 65–≤85 years (144/545, 26.4%); pediatric patients < 18 years had a higher serious AE likelihood (40/545, 7.3% vs. 10/540, 1.9% non-serious), while those > 85 years had a lower proportion (11/545, 2.0% vs. 19/540, 3.5%). Reporters: consumers accounted for 58.7% of non-serious AEs but only 24.8% of serious ones (317/540 vs. 135/545), whereas health professionals (including Health Professional, Physician, and Other Health Professional) contributed 69.0% of serious AEs and 27.2% of non-serious ones (197 + 94+85/545 vs. 14 + 117+16/540).

3.2 Signal strength detection at the SOC level

The reported proportions for tobramycin/dexamethasone-related AEs at the SOC level were calculated and visualized in Fig. 2. Eye Disorders accounted for the largest proportion (44.55%), far surpassing other System Organ Classes (SOCs). The next most common SOCs were General Disorders and Administration Site Conditions (10.93%), Injury, Poisoning and Procedural Complications (9.17%), Skin and Subcutaneous Tissue Disorders (5.15%), and Infections and Infestations (4.52%). SOCs such as Nervous System Disorders (4.1%) and Gastrointestinal Disorders (3.06%) had low proportions, while rare events were seen in Hepatobiliary Disorders (0.03%) and Congenital, Familial and Genetic Disorders (0.03%).

Figure 3 shows the signal strengths of Tobramycin/dexamethason across various SOC levels in the FAERS database (Supplementary Table 1). Eye Disorders was the most frequently reported category (n =

1465), and it also exhibited the strongest pharmacovigilance signal (ROR 39.41, 95% CI 36.79 – 42.21). The second strongest signal was observed for Ear And Labyrinth Disorders (ROR 3.98, 95% CI 3.05 – 5.18; n = 56), followed by Immune System Disorders (ROR 2.08, 95% CI 1.65 – 2.62; n = 75) and Product Issues (ROR 1.71, 95% CI 1.39 – 2.11; n = 90). In contrast, signals lacked statistical significance (lower ROR 95% CI limit ≤ 1) for multiple SOCs, including Skin And Subcutaneous Tissue Disorders (ROR 0.95), Injury, Poisoning And Procedural Complications (ROR 0.88), and Infections And Infestations (ROR 0.86).

3.3 Signal strength detection at the Preferred Terms level

We systematically categorized and ranked all AEs related to tobramycin/dexamethasone by report frequency. Figure 4 displays the number of reports for different PTs related to tobramycin/dexamethasone in the FAERS database (top 50) (Supplementary Table 2). Eye Disorders emerged as the most prominent SOC, with most of the top-ranked PTs falling under this category. Eye Pain was the most frequently reported event (a = 117) with a notably high ROR of 43.46 (95% CI: 36.13 ~ 52.28). Other highly prevalent ocular events included Vision Blurred (a = 98, ROR = 13.97, 95% CI: 11.43 ~ 17.08), Ocular Hyperaemia (a = 94, ROR = 40.95, 95% CI: 33.35 ~ 50.28), Eye Irritation (a = 88, ROR = 33.52, 95% CI: 27.11 ~ 41.43), Visual Impairment (a = 50, ROR = 7.53, 95% CI: 5.69 ~ 9.96), Eye Swelling (a = 45, ROR = 23.42, 95% CI: 7.44 ~ 31.43), Photophobia (a = 43, ROR = 44.89, 95% CI: 33.22 ~ 60.6), Eye Pruritus (a = 38, ROR = 24.03, 95% CI: 17.45 ~ 33.1), Conjunctival Hyperaemia (a = 36, ROR = 193.61, 95% CI: 139.15 ~ 269.39), Visual Acuity Reduced (a = 36, ROR = 19.17, 95% CI: 13.8 ~ 26.63), Ocular Hypertension (a = 36, ROR = 380.03, 95% CI: 272.65 ~ 529.71), Lacrimation Increased (a = 32, ROR = 21.27, 95% CI: 15.01 ~ 30.13), Glaucoma (a = 32, ROR = 21.27, 95% CI: 15.04 ~ 30.03), Cataract (a = 28, ROR = 9.18, 95% CI: 6.33 ~ 13.31), Eye Disorder (a = 27, ROR = 15.76, 95% CI: 10.79 ~ 23.02), Corneal Opacity (a = 25, ROR = 358.33, 95% CI: 240.77 ~ 533.28). Serious ocular symptoms in this SOC featured extremely strong signals: Corneal Exfoliation (a = 14, ROR = 3243.77, 95% CI: 1829.16 ~ 5752.41). For the Investigations SOC, IOP Increased was a key event (a = 62, ROR = 90.59, 95% CI: 70.42 ~ 116.55). In the Nervous System Disorders SOC, the main reported events were Headache (a = 49) with a low ROR of 1.47 (95% CI: 1.11 ~ 1.95) and Hypersensitivity (a = 48) with a low ROR of 4.91 (95% CI: 3.69 ~ 6.53).

3.4 PT analysis in gender, age, and reported population subgroups

We conducted a gender-differential analysis using the ROR method, with results in the forest plot in Fig. 5. Females were found to have a relatively elevated risk of PTs including Drug Ineffective (Female/Male: 65/26, ROR = 1.3, 95% CI: 0.82 – 2.06), Eye Irritation (Female/Male: 59/24, ROR = 1.28, 95% CI: 0.79 – 2.06), Visual Impairment (Female/Male: 41/10, ROR = 2.14, 95% CI: 1.07–4.28), Hypersensitivity (Female/Male: 34/12, ROR = 1.47, 95% CI: 0.76–2.85), Lacrimation Increased (Female/Male: 23/7, ROR = 1.7, 95% CI: 0.73–3.98), Cataract (Female/Male: 21/4, ROR = 2.73, 95% CI: 0.93–7.96). In contrast, males exhibited a relatively higher representation in reports of IOP Increased (Female/Male: 26/30, ROR = 0.44, 95% CI: 0.26–0.75), Conjunctival Hyperaemia (Female/Male: 16/20, ROR = 0.41, 95% CI: 0.21 – 0.79), Glaucoma (Female/Male: 15/17, ROR = 0.45, 95% CI:0.22–0.91), Corneal Opacity (Female/Male: 11/13, ROR = 0.43, 95% CI: 0.19 – 0.97), though these signals lacked statistical significance. Notably, most core ocular AEs of tobramycin/dexamethasone showed no statistically significant gender differences in ROR, as the 95% CIs of their ROR values all included 1.

As shown in Supplementary Fig. 1a spectrum of core ocular AEs were statistically significant in both males and females, encompassing Eye Pain, Ocular Hyperaemia, Vision Blurred, IOP Increased, Eye Irritation, Conjunctival Hyperaemia, Photophobia, Ocular Hypertension, Glaucoma, Eye Swelling, Visual Acuity Reduced, Headache, Condition Aggravated, Hypersensitivity, Eye Pruritus, Eye Disorder, Endophthalmitis, Visual Impairment, Dizziness, Rash. Males predominantly manifested Corneal Opacity, Eye Inflammation, Ocular Discomfort, Dry Eye, Keratic Precipitates. Conversely, females exhibited a higher propensity for Lacrimation Increased, Cataract. Males predominantly manifested PTs with ultra-high RORs, such as Conjunctival Hyperaemia (Male: ROR = 275.12, 95% CI: 176.19 – 429.61; Female: ROR = 169.86, 95% CI: 103.59 – 278.52), Ocular Hypertension (Male: ROR = 511.8, 95% CI: 314.88 – 831.88; Female: ROR = 338.93, 95% CI: 209.22 – 549.08) and IOP Increased (Male: ROR = 141.27, 95% CI: 98.14 – 203.36; Female: ROR = 67.17, 95% CI: 45.58 – 98.97). Conversely, females showed a higher propensity for severe ocular events like Endophthalmitis (Female: ROR = 164.15, 95% CI: 104.24 – 258.49; Male: ROR = 104.82, 95% CI: 56.13 – 195.73) .

As shown in Supplementary Fig. 2, across age subgroups, AEs presented distinct distribution patterns. In the < 18 years group (with small report volumes), PTs with drastically elevated RORs included IOP Increased (N = 5, ROR = 312.13, 95% CI: 136.16 – 715.49), Ocular Hypertension (N = 5, ROR = 615.22, 95% CI: 247.24 – 1530.88), Cellulitis Orbital (N = 2, ROR = 817.96, 95% CI: 195.69 – 3418.97), Glaucoma (N = 5, ROR = 369.11, 95% CI: 149.19 – 913.21). For the 18–<65 years group (the largest subgroup by report count), core ocular AEs combined high frequency and strong signals: Eye Pain (N = 52, ROR = 56.8, 95% CI: 43.01 – 74.99), Ocular Hyperaemia (N = 37, ROR = 45.82, 95% CI: 33.03 – 63.57), IOP Increased (N = 31, ROR = 194.41, 95% CI: 135.87 – 278.18), Ocular Hypertension (N = 22, ROR = 704.71, 95% CI: 458.5 – 1083.14). In the ≥ 65 years group, severe age-associated ocular reactions like Corneal Exfoliation (N = 11, ROR = 7238.48, 95% CI: 3499.33 – 14973.03), Conjunctival Hyperaemia (N = 12, ROR = 229.74, 95% CI: 129.39 – 407.94), Photophobia (N = 14, ROR = 82.23, 95% CI: 48.42 – 139.63) and Eye Pain (N = 34, ROR = 47.33, 95% CI: 30.57 – 76.72) exhibited significant signals.

As shown in Supplementary Fig. 3, among the reporting population stratified into Health professional and Consumer subgroups, AEs displayed distinct characteristic patterns. In the Health professional subgroup, moderate-report-count PTs showed strong signals: IOP Increased (N = 22, ROR = 67.25, 95% CI: 44.13 – 102.55), Eye Inflammation (N = 10, ROR = 45.74, 95% CI: 24.53 – 85.26) and Photophobia (N = 17, ROR = 37.28, 95% CI: 23.09 – 60.17). In the Consumer subgroup (with higher overall report volumes), several PTs had extremely high RORs: Lipogranuloma (N = 7, ROR = 8248.13, 95% CI: 3476.34 – 20047.32), Endophthalmitis (N = 23, ROR = 196.53, 95% CI: 129.52 – 298.22), and Anterior Chamber Flare (N = 6, ROR = 1099.34, 95% CI: 482.44 – 2505.1). Core ocular events like Eye Pain (N = 35, ROR = 108.03, 95% CI: 57.68 – 201.71) also showed robust signals in this subgroup.

3.5 Clinical prioritization of signals

Based on the clinical prioritization of the top 50 Preferred Terms (PTs) associated with tobramycin/dexamethasone in the FAERS database, AEs were categorized into medium-priority and low-priority levels (Supplementary Table 3). First, no high-priority AEs were found. Medium-priority PTs predominantly include: Eye Pain with a strong signal (N = 120, ROR = 44.29, 95% CI: 36.9 – 53.15), Vision Blurred (N = 98, ROR = 13.86, 95% CI: 11.34 – 16.95), Ocular hyperaemia (N = 95, ROR = 40.79, 95% CI: 33.26 – 50.3), Eye irritation (N = 88, ROR = 33.17 95% CI: 26.83 – 41), IOP increased (N = 63, ROR = 92.08, 95% CI: 71.72 – 118.23), Ocular hypertension (N = 36, ROR = 34.55, 95% CI: 268.75 – 522).Low-priority PTs predominantly include: Drug ineffective (N = 97, ROR = 1.38, 95% CI: 1.13 – 1.69), Headache (N = 49, ROR = 1.46, 95% CI: 1.1 – 1.93), Ocular discomfort (N = 23, ROR = 43.98, 95% CI: 29.17 – 66.32), Eye inflammation (N = 21, ROR = 43.74, 95% CI: 28.47 – 67.22), Keratitis (N = 17, ROR = 109.35, 95% CI: 67.79 – 176.38), Corneal oedema (N = 16, ROR = 131.59, 95% CI: 80.37 – 215.46), Dacryostenosis acquired (N = 13, ROR = 186.78, 95% CI: 108.02 – 322.97).

3.6 TTO of tobramycin/dexamethasone-related AEs

From the FAERS database, onset times of tobramycin/dexamethasone-related AEs were analyzed after excluding missing/incorrect data, with 816 eligible cases. Weibull analysis (Table 3) showed a median time-to-onset (TTO) of 13 days (IQR: 2 – 15 days), a TTO range of 1 – 1900 days, scale parameter (α) = 15.204 (95% CI: 13.073 – 17.335), and shape parameter (β) = 0.521 (95% CI: 0.498 – 0.545). β < 1 indicates an Early-Life Failure pattern with a decreasing failure rate.

As shown in Fig. 6, 88.08% of AEs occurred within the first month of treatment, with incidence gradually declining thereafter; late-onset AEs are relatively rare. Categorized by temporal profile (Supplementary Table 4), early-onset AEs (0 – 7 days) were predominantly ocular: Eye pain (N = 19) and Vision blurred (N = 19) were most frequent, followed by Ocular hyperaemia (N = 15), Ocular hypertension (N = 13), and Eye swelling (N = 12). Mid-onset AEs (> 7 – 30 days) had fewer reports: IOP increased (N = 8) was most common, followed by Eye pain (N = 7) and Ocular hypertension (N = 5), with Eye swelling (N = 2) rarely reported.

4. Discussion

Consistent with the drug's topical ophthalmic indication, our analysis identified Eye Disorders as the predominant SOC, accounting for 44.55% of all AEs – far exceeding other organ systems. Core PTs with strong disproportionality signals included Eye Pain (N = 117, ROR = 43.46), Vision Blurred (N = 98, ROR = 13.97), and Ocular Hyperaemia (N = 94, ROR = 40.95). Eye Pain and Ocular Hyperaemia have been implicated in tobramycin-associated AEs in prior investigations(20, 21). Consistent with FDA-approved labeling, tobramycin-related AEs occur in < 4% of patients, predominantly including eye pain, eyelids pruritus, eyelid edema, and conjunctival hyperemia. Similarly, vision decreased (2.4%) was also documented among the 9% of patients enrolled in the 0.5% levofloxacin clinical trial(22). Notably, IOP Increased (N = 62, ROR = 90.59) and Ocular Hypertension (N = 36, ROR = 380.03) exhibited extremely high signal strengths, confirming the well-documented glucocorticoid-associated risk of elevated IOP(23–27).

These findings reinforce the importance of routine IOP monitoring in patients receiving prolonged treatment, particularly those with preexisting glaucoma or glaucoma susceptibility.

Beyond expected reactions, our study identified several PTs with strong signals that warrant heightened clinical vigilance, including Corneal Exfoliation (N = 14, ROR = 3243.77) and Conjunctival Hyperaemia (N = 36, ROR = 196.92). While these events are rare, their ultra-high RORs suggest a potential causal link to the drug—likely related to dexamethasone-induced epithelial barrier disruption or tobramycin-associated ocular surface toxicity(20, 28). This extends prior case reports of severe corneal damage associated with tobramycin/dexamethasone, highlighting the need for enhanced vigilance for corneal integrity in clinical practice.

Stratified analyses revealed distinct risk patterns across demographic and reporter subgroups, offering guidance for targeted monitoring strategies: Females accounted for the majority of total reports (61.5%) and non-serious AEs (68.1%), while males exhibited higher risks of severe ocular events with clinically meaningful RORs, including IOP Increased (Male ROR = 141.27 vs. Female ROR = 67.17) and Ocular Hypertension (Male ROR = 511.8 vs. Female ROR = 338.93). Evidence indicates that estrogen may serve as a potential therapeutic agent for glaucoma, as it exerts ocular protective effects against glaucoma-induced damage and reduces IOP(29)—a mechanism that may partially explain the higher susceptibility to IOP elevation in male patients. These gender-specific disparities are likely attributable to sex-related differences in glucocorticoid sensitivity, consistent with previous reports,(30) thereby emphasizing the need for intensified IOP monitoring in male patients receiving tobramycin/dexamethasone therapy. A U-shaped risk pattern was observed: pediatric patients < 18 years (4.6% of total reports) had a disproportionately high proportion of serious AEs (7.3%), with markedly elevated reporting odds ratios (RORs) for ocular hypertension (ROR = 615.22) and glaucoma (ROR = 369.11). This heightened risk is likely attributed to the ability of glucocorticoids to alter the morphological and biological properties of the trabecular meshwork, inhibit aqueous humor outflow, and thereby increase IOP—with steroids exerting a more pronounced effect on the immature trabecular meshwork of pediatric patients(5). Elderly patients aged ≥ 65 years (22.2% of total reports) exhibited strong safety signals for age-related severe adverse reactions, including corneal exfoliation (ROR = 7238.48) and photophobia (ROR = 82.23). This heightened risk is attributed to age-associated structural and functional changes in the ocular surface and corneal tissues, which can predispose individuals to dry eye disease and thereby impair the integrity of the ocular surface and its associated glands(31). Adults 18–<65 years (31.9% of total reports) had the highest overall serious AE rate (43.5%), with core ocular AEs (e.g., Eye Pain, ROR = 56.8; IOP Increased, ROR = 194.41; Ocular Hypertension, ROR = 704.71) combining high frequency and signal strength. Health professionals (including health professional, physician, other health professional) accounted for 68.9% of serious AE reports, compared to only 27.3% of non-serious reports, while consumers dominated non-serious reports (58.7%). This discrepancy underscores the tendency for severe reactions to be formally reported by healthcare providers, highlighting the value of integrating clinical practice reports into pharmacovigilance efforts.

The TTO analysis revealed a median onset time of 13 days (IQR: 2–15 days), with 88.08% of populational AEs occurring within the first month of treatment—consistent with an "Early-Life Failure" pattern (Weibull shape parameter $\beta = 0.521 < 1$). Early-onset AEs (0–7 days) were dominated by acute ocular irritation (e.g., Eye Pain, N = 19; Vision Blurred, N = 19), while mid-onset reactions (> 7–30 days) included IOP Increased (N = 8)—a delayed effect of glucocorticoid exposure(32–34). These findings support the need for intensified monitoring in the first month of treatment: acute irritation should be assessed within the first week, while IOP should be measured regularly during the first month, especially in long-term users.

Pre-treatment screening should prioritize glaucoma and corneal disease; IOP and corneal integrity should be monitored routinely (weekly for the first month, then monthly for prolonged use). Pediatric and elderly patients require more frequent follow-up, while male patients should be closely monitored for IOP elevation. Patients should be educated on early warning signs (e.g., persistent eye pain, vision changes) to enable timely intervention. The strong signals for rare severe PTs (e.g., Corneal Exfoliation) warrant inclusion in drug labeling to enhance clinician awareness. Subgroup-specific risk information (e.g., pediatric and geriatric vulnerability) should be integrated into prescribing guidelines to support personalized risk-benefit assessment.

This study inherits inherent limitations of spontaneous reporting systems: (1) Reporting bias favoring severe or novel reactions may overestimate the incidence of rare AEs; (2) Missing data on dose, treatment duration, and concurrent ocular medications preclude analysis of dose-response relationships or confounding factors; (3) Disproportionality signals indicate statistical association rather than definitive causality, requiring confirmatory studies for rare PTs; (4) Lack of long-term follow-up data limits characterization of very late-onset reactions (e.g., > 1 year). Despite these limitations, the large sample size, long study period, and multidimensional analysis provide robust real-world evidence to complement controlled trial data.

5. Conclusions

This large-scale pharmacovigilance study systematically characterizes the real-world safety profile of tobramycin/dexamethasone using FAERS data, confirming that ocular disorders are the core adverse reactions—with strong signals for both known risks (e.g., eye Pain, IOP increase, glaucoma) and underrecognized severe events (e.g., corneal exfoliation, conjunctival hyperaemia). Subgroup analyses reveal distinct risk patterns: males are more prone to IOP elevation and corneal damage, pediatric and elderly patients face heightened serious AE risks, and health professional reports capture more severe reactions. Temporal analysis identifies the first month as the critical monitoring window, with late-onset AEs emphasizing the need for prolonged surveillance in high-risk populations. These findings enhance clinical vigilance, guide personalized monitoring strategies, and support the optimization of post-marketing safety management for this widely used ophthalmic formulation. Future research should validate causal links for rare AEs and explore dose-response relationships to further refine risk stratification.

Abbreviations

Abbreviations	Full name
AE	Adverse Event
AEs	Adverse Events
BCPNN	Bayesian Confidence Propagation Neural Network
CASEID	Case Identifier
CI	Confidence interval
DEMO	Demographic and Administrative Records
DRUG	Drug Exposure Details
FAERS	Food and Drug Administration Adverse Event Reporting System
FDA	Food and Drug Administration
IME/DME	Important Medical Event/Designated Medical Event
INDI	Indications for Use
IOP	Intraocular pressure
IQR	Interquartile range
MedDRA	Medical Dictionary for Regulatory Activities
MGPS	Multi-item Gamma Poisson Shrinker
OUTC	Patient Clinical Outcomes
PRR	Proportional Reporting Ratio
PS	Primary Suspect
PT	Preferred Term
PTs	Preferred Terms
REAC	MedDRA-coded Adverse Reaction Information
READUS-PV	Reporting of a Disproportionality Analysis for Drug Safety Signal Detection Using Individual Case Safety Reports in PharmacoVigilance
ROR	Reporting Odds Ratio
RPSR	Report Source Metadata
SOC	System Organ Class
THER	Drug Therapy Timelines
TTO	Time-to-Onset

Abbreviations	Full name
WSP	Weibull Shape Parameter

Declarations

Ethics approval and consent to participate

This article does not contain any studies with human or animal participants. There are no human participants in this article and informed consent is not required.

Consent for publication

Not applicable.

Author Contributions

WWZ contributed to conceptualization and supervision. HGW contributed to writing, review and editing. SNW and WQH contributed to the implementation of formal analyses. ZDD contributed to statistical analysis and validation. All authors contributed to the article and approved the submitted version.

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Competing interests

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

Availability of data and material

The FDA Adverse Event Reporting System data are publicly available and can be found here: https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-eventreporting-system-faers/fda-

adverse-
event-reporting-system-faers-public-dashboard. The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

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Tables

Table 1
Clinical characteristics of reports with tobramycin/dexamethasone from the FAERS database.

Characteristics	**Number(N)**	**Proportion(%)**
Number of reports	1085	100
Gender		
Female	667	61.5
Male	333	30.7
Missing	85	7.8
Age (years)		
< 18	50	4.6
≥ 18 and < 65	346	31.9
≥ 65 and ≤ 85	241	22.2
> 85	30	2.8
Missing	418	38.5
Weight (kg)		
< 50	40	3.7
≥ 50 and ≤ 100	229	21.1
> 100	10	0.9
Missing	806	74.3
Reported person		
Consumer	452	41.7
Physician	211	19.4
Health Professional	211	19.4
Pharmacist	33	3
Other	101	9.3
Lawyer	4	0.4
Missing	73	6.7
Outcome Code		
Death	7	0.6

Characteristics	Number(N)	Proportion(%)
Disability	32	2.9
Hospitalization	102	9.4
Life-Threatening	6	0.6
Other	395	36.4
Required Intervention	3	0.3
Missing	540	49.8
Serious cases		
No	540	49.8
Yes	545	50.2
Fatal cases		
No	1078	99.4
Yes	7	0.6
Main reported country		
United States	507	46.7
China	204	18.8
France	59	5.4
Spain	35	3.2
Canada	17	1.6
United Kingdom	15	1.4
Other Countries	248	22.9

Table 2
Clinical characteristics of reports with tobramycin/dexamethasone between fatal and non-fatal occurred from the FAERS database.

Gender	Not serious(N = 540)	Serious(N = 545)	Overall(N = 1085)
Female	368 (68.1%)	299 (54.9%)	667 (61.5%)
Male	124 (23.0%)	209 (38.3%)	333 (30.7%)
missing	48 (8.9%)	37 (6.8%)	85 (7.8%)
Weight (kg)			
< 50	8 (1.5%)	32 (5.9%)	40 (3.7%)
> 100	4 (0.7%)	6 (1.1%)	10 (0.9%)
≥ 50 and ≤ 100	74 (13.7%)	155 (28.4%)	229 (21.1%)
missing	454 (84.1%)	352 (64.6%)	806 (74.3%)
Age (years)			
< 18	10 (1.9%)	40 (7.3%)	50 (4.6%)
> 85	19 (3.5%)	11 (2.0%)	30 (2.8%)
≥ 18 and < 65	109 (20.2%)	237 (43.5%)	346 (31.9%)
≥ 65 and ≤ 85	97 (18.0%)	144 (26.4%)	241 (22.2%)
missing	305 (56.5%)	113 (20.7%)	418 (38.5%)
Reported person			
Consumer	317 (58.7%)	135 (24.8%)	452 (41.7%)
Health Professional	14 (2.6%)	197 (36.1%)	211 (19.4%)
Lawyer	4 (0.7%)	0 (0%)	4 (0.4%)
Physician	117 (21.7%)	94 (17.2%)	211 (19.4%)
missing	53 (9.8%)	20 (3.7%)	73 (6.7%)
Other Health Professional	16 (3.0%)	85 (15.6%)	101 (9.3%)
Pharmacist	19 (3.5%)	14 (2.6%)	33 (3.0%)
Outcome Code			
Death	0 (0%)	7 (1.3%)	7 (0.6%)
Disability	0 (0%)	32 (5.9%)	32 (2.9%)

Gender	Not serious(N = 540)	Serious(N = 545)	Overall(N = 1085)
Hospitalization	0 (0%)	102 (18.7%)	102 (9.4%)
Life-Threatening	0 (0%)	6 (1.1%)	6 (0.6%)
Required Intervention	0 (0%)	3 (0.6%)	3 (0.3%)
Other Serious Outcome	0 (0%)	395 (72.5%)	395 (36.4%)
missing	540 (100%)	0 (0%)	540 (49.8%)

Table 3
Time-to-onset analysis for tobramycin/dexamethasone-related signals using the Weibull distribution test.

Cases (N)	TTO(days)		Weibull distribution				Failure Type	Failure Rate Trend
			Scale parameter		Shape parameter			
Media (IQR)	Min-Max	α	95% CI	β	95% CI			
816	13(2–15)	1-1900	15.204	13.073–17.335	0.521	0.498–0.545	Early-Life Failures	Decreasing

N, number of cases with available time-to-onset; IQR, interquartile range; TTO, Time-to-onset. A TTO of 0 days means that the adverse event happens within the day of treatment.

Figures

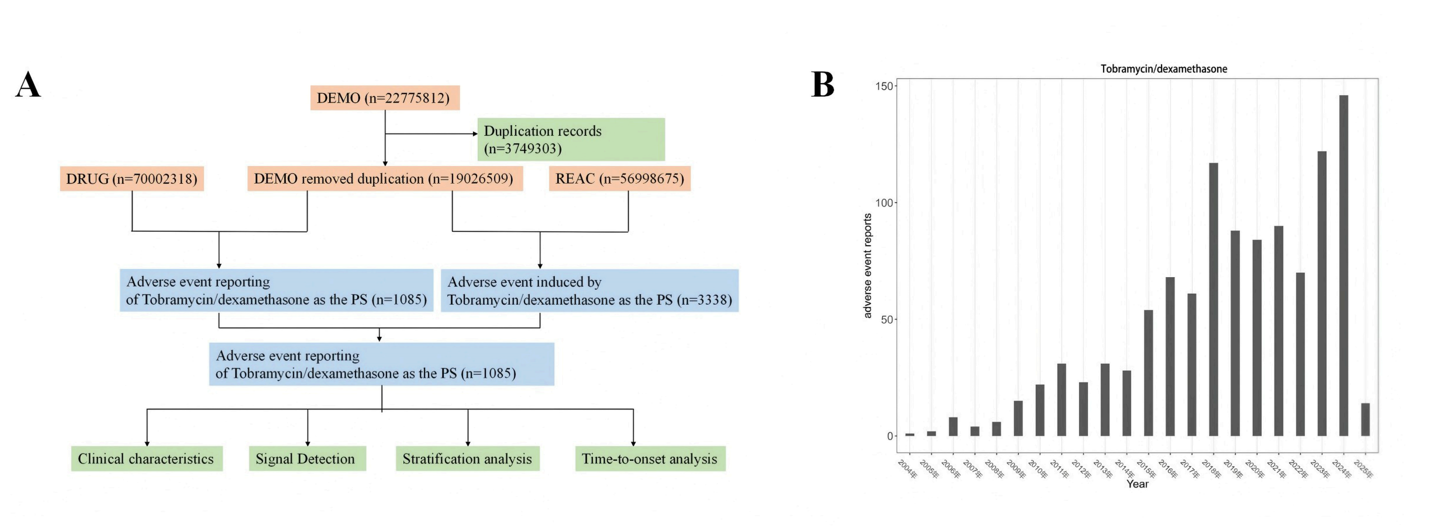

Figure 1

(A) The flow diagram of selecting tobramycin/dexamethasone-related AEs from FAERS database. (B) The annual distribution of tobramycin/dexamethasone-related AEs reports from 2004 Q1 to 2025 Q2. DEMO, Demographic and administrative records; DRUG, Drug exposure information; REAC, Adverse reaction specifics coded in MedDRA; AEs, adverse events.

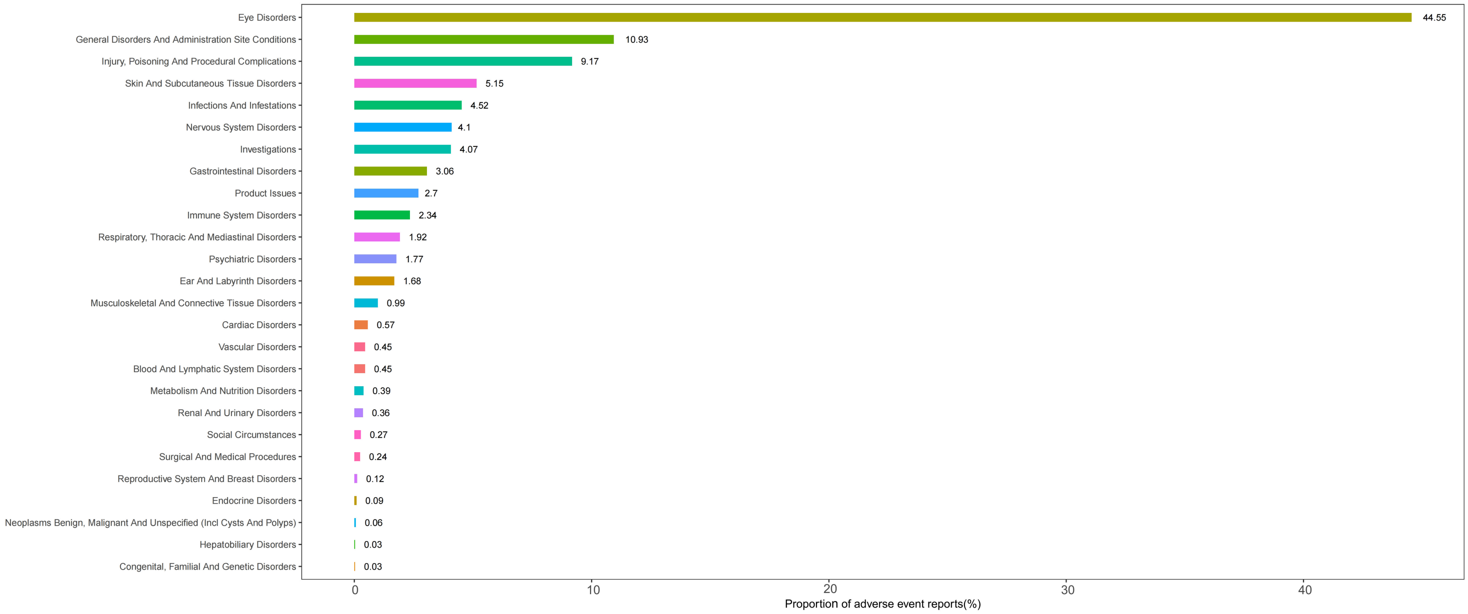

Figure 2

The bar chart illustrates significant variability in adverse event reporting proportions across SOCs. SOCs, System Organ Classes.

SOC	N	ROR(95% CI)
Eye Disorders	1465	39.41(36.79~42.21
Ear And Labyrinth Disorders	56	3.98(3.05~5.18
Immune System Disorders	75	2.08(1.65~2.62
Product Issues	90	1.71(1.39~2.11
Skin And Subcutaneous Tissue Disorders	170	0.95(0.82~1.11
Injury, Poisoning And Procedural Complications	304	0.88(0.78~0.99
Infections And Infestations	149	0.86(0.73~1.01
Investigations	134	0.65(0.54~0.77
General Disorders And Administration Site Conditions	359	0.58(0.52~0.64
Social Circumstances	9	0.58(0.3~1.13
Nervous System Disorders	137	0.47(0.39~0.56
Respiratory, Thoracic And Mediastinal Disorders	64	0.4(0.31~0.51
Endocrine Disorders	3	0.36(0.11~1.1
Gastrointestinal Disorders	102	0.34(0.28~0.42
Psychiatric Disorders	59	0.31(0.24~0.4
Blood And Lymphatic System Disorders	15	0.26(0.16~0.44
Cardiac Disorders	19	0.21(0.14~0.34
Vascular Disorders	15	0.21(0.13~0.35
Renal And Urinary Disorders	12	0.19(0.11~0.33
Musculoskeletal And Connective Tissue Disorders	33	0.18(0.13~0.26
Metabolism And Nutrition Disorders	13	0.18(0.1~0.31
Surgical And Medical Procedures	8	0.18(0.09~0.36
Reproductive System And Breast Disorders	4	0.14(0.05~0.36
Congenital, Familial And Genetic Disorders	1	0.1(0.01~0.69
Hepatobiliary Disorders	1	0.03(0~0.23
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	2	0.02(0.01~0.09

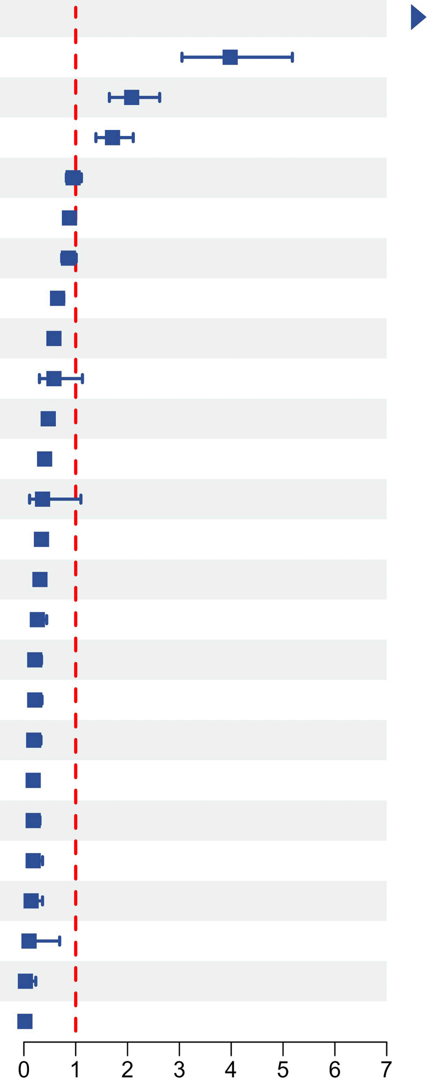

Figure 3

The forest plot displays the 26 adverse event terms (SOC), showing the ROR and 95% CI, ordered by reporting frequency. N, number of cases; SOC, System Organ Class; PT, Preferred Term; ROR, reporting odds ratio; CI, confidence interval.

SOC	PT(Preferred Term)	a	ROR(95% CI)
Eye Disorders	Eye Pain	117	43.46(36.13~52.28
Eye Disorders	Vision Blurred	98	13.97(11.43~17.08
Eye Disorders	Ocular Hyperaemia	94	40.95(33.35~50.28
Eye Disorders	Eye Irritation	88	33.52(27.11~41.43
Investigations	Intraocular Pressure Increased	62	90.59(70.42~116.55
Eye Disorders	Visual Impairment	50	7.53(5.69~9.96
Nervous System Disorders	Headache	49	1.47(1.11~1.95
Immune System Disorders	Hypersensitivity	48	4.91(3.69~6.53
Eye Disorders	Eye Swelling	45	23.42(17.44~31.43
Eye Disorders	Photophobia	43	44.89(33.22~60.68
Eye Disorders	Eye Pruritus	38	24.03(17.45~33.1
Eye Disorders	Conjunctival Hyperaemia	36	193.61(139.15~269.39
Eye Disorders	Visual Acuity Reduced	36	19.17(13.8~26.63
Eye Disorders	Ocular Hypertension	36	380.03(272.65~529.71
Eye Disorders	Lacrimation Increased	32	21.27(15.01~30.13
Eye Disorders	Glaucoma	32	31.34(22.12~44.41
General Disorders And Administration Site Conditions	Condition Aggravated	31	2.03(1.42~2.89
Infections And Infestations	Endophthalmitis	31	98.41(69.03~140.32
Eye Disorders	Cataract	28	9.18(6.33~13.31
Eye Disorders	Eye Disorder	27	15.76(10.79~23.02
Injury, Poisoning And Procedural Complications	Product Use In Unapproved Indication	27	2.28(1.56~3.33
Nervous System Disorders	Dizziness	25	0.94(0.63~1.39
Eye Disorders	Corneal Opacity	25	358.33(240.77~533.28
Product Issues	Product Quality Issue	25	3.33(2.25~4.94
Skin And Subcutaneous Tissue Disorders	Rash	23	0.95(0.63~1.43
Gastrointestinal Disorders	Nausea	23	0.55(0.36~0.82
Skin And Subcutaneous Tissue Disorders	Erythema	23	2.05(1.36~3.08
Eye Disorders	Ocular Discomfort	23	44.89(29.77~67.69
Eye Disorders	Dry Eye	20	8.63(5.56~13.4
Eye Disorders	Eye Inflammation	20	42.5(27.37~66.01
Skin And Subcutaneous Tissue Disorders	Pruritus	20	0.99(0.64~1.54
Eye Disorders	Eyelid Oedema	19	28.95(18.44~45.47
Eye Disorders	Uveitis	18	26.42(16.62~42
Eye Disorders	Eye Discharge	17	33.46(20.77~53.92
Eye Disorders	Keratitis	17	110.43(68.46~178.14
Ear And Labyrinth Disorders	Tinnitus	16	6.53(3.99~10.67
Eye Disorders	Corneal Oedema	16	133.45(81.5~218.52
Investigations	Blood Pressure Increased	16	1.96(1.2~3.2
Infections And Infestations	Conjunctivitis	16	16.8(10.28~27.47
Injury, Poisoning And Procedural Complications	Product Dose Omission Issue	16	0.62(0.38~1.01
General Disorders And Administration Site Conditions	Pain	15	0.45(0.27~0.74
Eye Disorders	Foreign Body Sensation In Eyes	15	46.95(28.25~78.02
Eye Disorders	Erythema Of Eyelid	15	55.24(33.24~91.81
General Disorders And Administration Site Conditions	Swelling Face	14	4.05(2.4~6.85
Immune System Disorders	Drug Hypersensitivity	14	1.32(0.78~2.24
Eye Disorders	Swelling Of Eyelid	14	50.92(30.1~86.14
Eye Disorders	Corneal Exfoliation	14	3243.77(1829.16~5752.41
Injury, Poisoning And Procedural Complications	Product Use Issue	13	1.36(0.79~2.34
Nervous System Disorders	Dysgeusia	13	3.15(1.82~5.42
Eye Disorders	Ulcerative Keratitis	13	88.92(51.5~153.52

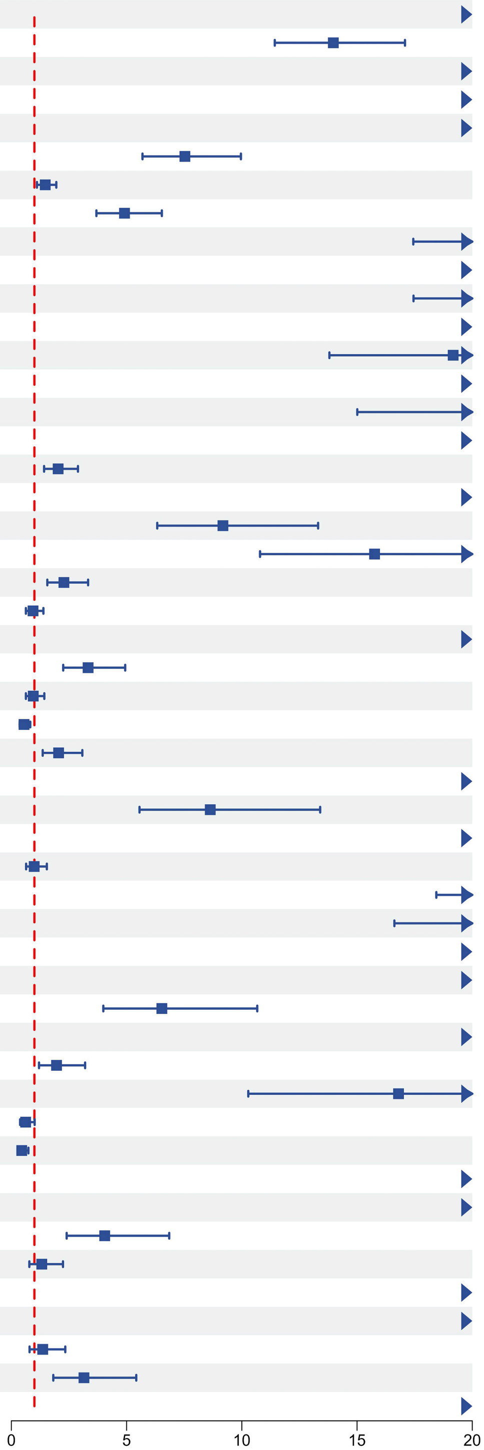

Figure 4

The forest plot displays the top 50 adverse event terms (PT), showing the ROR and 95% CI, ordered by reporting frequency. N, number of cases; SOC, System Organ Class; PT, Preferred Term; ROR, reporting odds ratio; CI, confidence interval.

soc	PT	FEMLAE/MALE	ROR(95% CI)
EYE DISORDERS	EYE PAIN	74 / 41	0.93(0.63−1.37)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	DRUG INEFFECTIVE	65 / 26	1.3(0.82−2.06)
EYE DISORDERS	VISION BLURRED	62 / 32	1(0.65−1.54)
EYE DISORDERS	EYE IRRITATION	59 / 24	1.28(0.79−2.06)
EYE DISORDERS	OCULAR HYPERAEMIA	56 / 37	0.77(0.51−1.18)
EYE DISORDERS	VISUAL IMPAIRMENT	41 / 10	2.14(1.07−4.28)
IMMUNE SYSTEM DISORDERS	HYPERSENSITIVITY	34 / 12	1.47(0.76−2.85)
NERVOUS SYSTEM DISORDERS	HEADACHE	31 / 15	1.07(0.57−1.99)
EYE DISORDERS	EYE SWELLING	28 / 16	0.9(0.49−1.67)
INVESTIGATIONS	INTRAOCULAR PRESSURE INCREASED	26 / 30	0.44(0.26−0.75)
EYE DISORDERS	EYE PRURITUS	25 / 12	1.08(0.54−2.15)
EYE DISORDERS	LACRIMATION INCREASED	23 / 7	1.7(0.73−3.98)
EYE DISORDERS	PHOTOPHOBIA	23 / 17	0.69(0.37−1.31)
EYE DISORDERS	VISUAL ACUITY REDUCED	21 / 15	0.72(0.37−1.4)
EYE DISORDERS	CATARACT	21 / 4	2.73(0.93−7.96)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	CONDITION AGGRAVATED	19 / 12	0.82(0.39−1.69)
INFECTIONS AND INFESTATIONS	ENDOPHTHALMITIS	19 / 10	0.98(0.45−2.12)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	OFF LABEL USE	17 / 9	0.97(0.43−2.19)
PRODUCT ISSUES	PRODUCT QUALITY ISSUE	17 / 6	1.47(0.58−3.73)
EYE DISORDERS	OCULAR HYPERTENSION	17 / 17	0.51(0.26−1.01)
EYE DISORDERS	EYE DISORDER	16 / 10	0.82(0.37−1.82)
EYE DISORDERS	CONJUNCTIVAL HYPERAEMIA	16 / 20	0.41(0.21−0.79)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	PRURITUS	16 / 5	1.66(0.6−4.53)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	RASH	15 / 8	0.97(0.41−2.29)
GASTROINTESTINAL DISORDERS	NAUSEA	15 / 4	1.94(0.64−5.86)
EYE DISORDERS	GLAUCOMA	15 / 17	0.45(0.22−0.91)
NERVOUS SYSTEM DISORDERS	DIZZINESS	15 / 9	0.86(0.37−1.97)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	PRODUCT USE IN UNAPPROVED INDICATION	15 / 7	1.11(0.45−2.72)
EYE DISORDERS	EYELID OEDEMA	14 / 5	1.45(0.52−4.03)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	ERYTHEMA	14 / 7	1.03(0.42−2.56)
EYE DISORDERS	ERYTHEMA OF EYELID	13 / 3	2.24(0.64−7.89)
IMMUNE SYSTEM DISORDERS	DRUG HYPERSENSITIVITY	13 / 2	3.37(0.76−14.95)
EYE DISORDERS	SWELLING OF EYELID	13 / 2	3.37(0.76−14.95)
EYE DISORDERS	EYE INFLAMMATION	12 / 9	0.69(0.29−1.63)
EYE DISORDERS	OCULAR DISCOMFORT	12 / 9	0.69(0.29−1.63)
EYE DISORDERS	EYE DISCHARGE	12 / 4	1.55(0.5−4.82)
INFECTIONS AND INFESTATIONS	CONJUNCTIVITIS	12 / 3	2.07(0.58−7.35)
EAR AND LABYRINTH DISORDERS	TINNITUS	11 / 5	1.14(0.39−3.28)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	PAIN	11 / 4	1.42(0.45−4.47)
EYE DISORDERS	CORNEAL OPACITY	11 / 13	0.43(0.19−0.97)
EYE DISORDERS	DRY EYE	11 / 8	0.71(0.28−1.76)
EYE DISORDERS	UVEITIS	10 / 8	0.64(0.25−1.63)
INVESTIGATIONS	BLOOD PRESSURE INCREASED	10 / 5	1.03(0.35−3.03)
EYE DISORDERS	KERATITIS	10 / 5	1.03(0.35−3.03)
PRODUCT ISSUES	PRODUCT DELIVERY MECHANISM ISSUE	10 / 2	2.59(0.57−11.83)
EYE DISORDERS	DACRYOSTENOSIS ACQUIRED	10 / 3	1.72(0.47−6.27)
PSYCHIATRIC DISORDERS	INSOMNIA	9 / 1	4.66(0.59−36.82)
EYE DISORDERS	CORNEAL DISORDER	9 / 3	1.55(0.42−5.74)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	ACCIDENTAL EXPOSURE TO PRODUCT	9 / 3	1.55(0.42−5.74)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	SWELLING FACE	9 / 5	0.93(0.31−2.78)

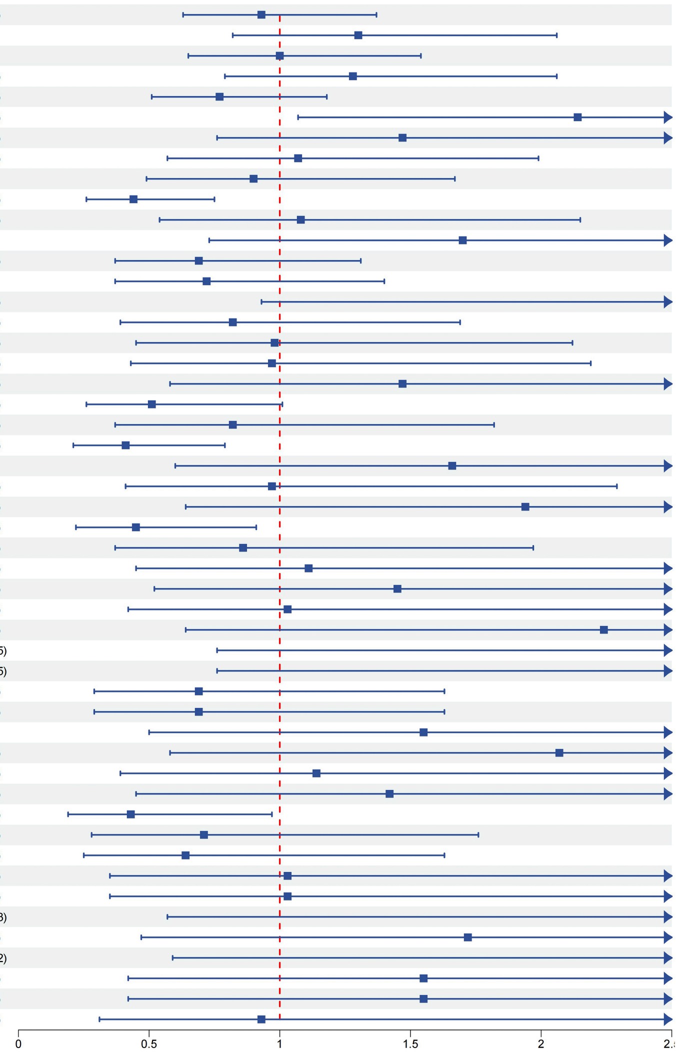

Figure 5

The forest plot displays the proportion of female to male occurrence for main adverse event terms (PT). SOC, System Organ Class; PT, Preferred Term; ROR, reporting odds ratio; CI, confidence interval

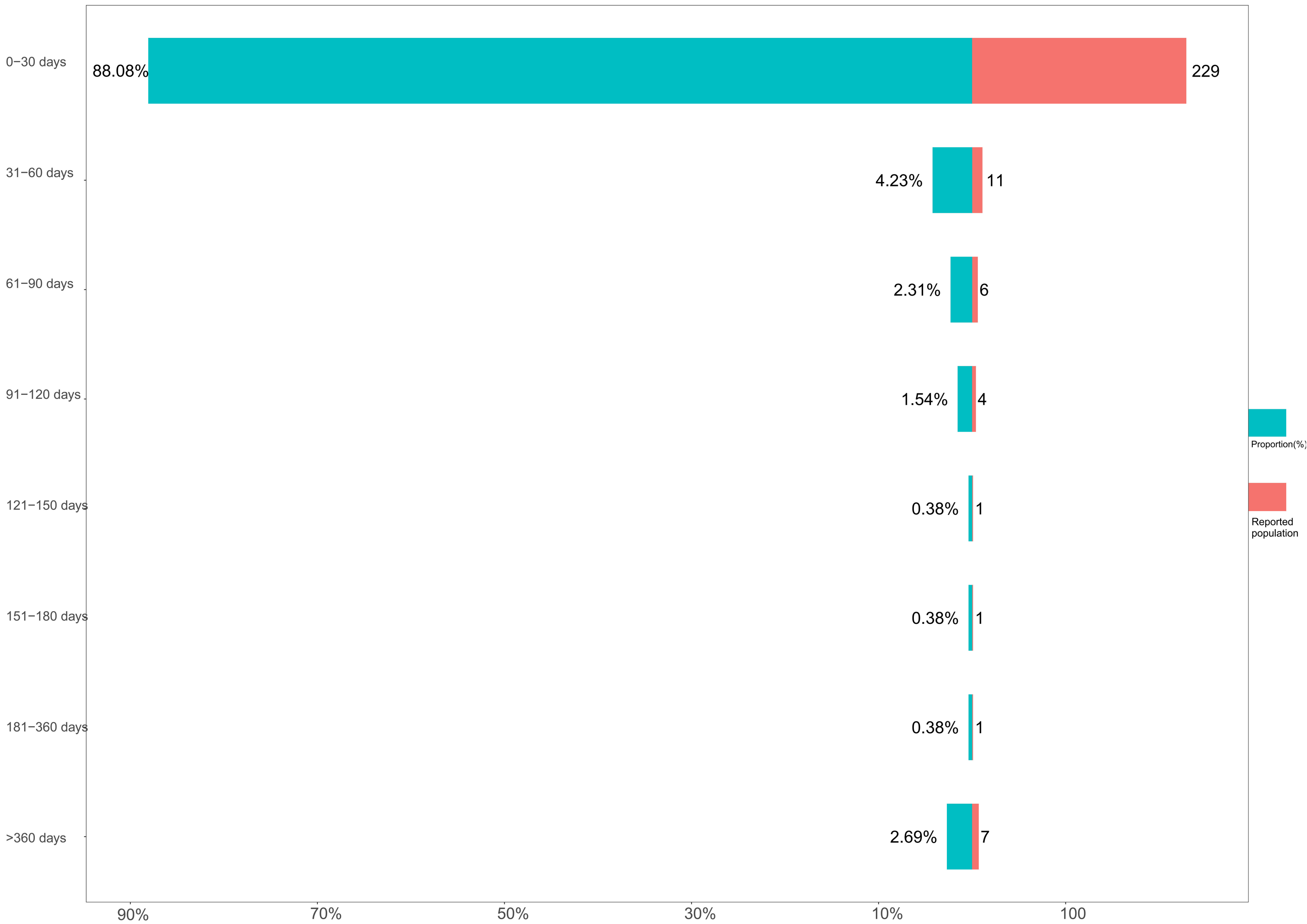

Figure 6

The bar chart illustrates time-to-onset populational distribution of tobramycin/dexamethasone-related AEs. AEs, adverse events.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable1.xlsx
- SupplementaryTable2.xlsx
- SupplementaryTable3.xlsx
- SupplementaryTable4.xlsx
- SupplementaryFigure1.jpg
- SupplementaryFigure2.jpg
- SupplementaryFigure3.jpg